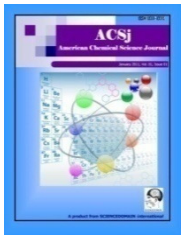

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Synthesis and Antimicrobial Activities of Novel Aminoalkylated 2*H*-benzotriazoles

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Authors' contributions

This work was carried out in collaboration among both the authors. Author SCJ designed and supervised the study. Author BB performed synthesis, material preparation, statistical analysis and other important studies.

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ABSTRACT

In view of generating new compounds for future drug development, we have synthesized some *N*-aminoalkylated derivatives of benzo[*d*][1,2,3]triazole by alkylating benzo[*d*][1,2,3]triazole in the presence of K_2CO_3/DMF using 1,6-dibromohexane to obtain the 2-(6-bromohexyl)-2*H*-benzo[*d*][1,2,3]triazole (3) as the one of the major product which was then used as an intermediate to synthesize a new series of compounds 4a-j. All the synthesized compounds were fully characterized on the basis of their detailed spectral studies and were evaluated for their antimicrobial activities *In vitro* against three Gram-positive bacteria (*Staphylococcus aureus, Bacillus subtilis* and *Staphylococcus epidermis*), four Gram-negative bacteria (*Echerichia coli, Pseudomonas aeuroginosa, Staphylococcus typhi and Klebsiella pneumoniae*) and four fungi (*Aspergillus niger*, *Aspergillus fumigatus, Candida albicans* and *Aspergillus flavus*) strains using Cup plate method.

Keywords: Antimicrobial activity; benzo[d][1,2,3]triazole; 1,6-dibromohexane; aliphatic/ heterocyclic secondary amines.

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1. INTRODUCTION

Heterocyclic compounds, a main class of pharmacologically active agents, are the basis of life and their synthesis has always been full of excitement and challenges. Nitrogen heterocycles in particular exhibit diverse biological and pharmacological activities due in part to the similarities with many natural and synthetic molecules with known biological activities. Development of novel, economically viable and efficient synthesis protocols for attractive heterocyclic scaffolds is perhaps the ultimate goal of synthetic organic chemists in search of new pharmaceutical lead structures.

Benzo-fused azoles containing three heteroatoms, specially, benzo[*d*][1,2,3]triazole, has received great attention for their chemical and biological properties and applications in the pharmaceutical industry. Vorozole, a nonsteroidal aromatase inhibitor, and alizapride, an antiemetic drug for the treatment of nausea and vomiting, contain a benzotriazole skeleton [1,2]. Recently, 1-substituted benzotriazole carboxylic acids have been identified as the first reported example of selective small-molecule agonists of the human orphan G-protein-coupled receptor GPR109b (HM74) [3]. Several novel benzotriazole derivatives also have their inhibitory properties against different kinases [4]. Also, many biologically active compounds containing of benzotriazole nucleus have been shown to display diverse and interesting biological and pharmacological activities [5-10]. Despite the tremendous development in benzotriazole chemistry, there is still a dearth of recent and concise reports on synthetic applications of benzotriazole for the development of heterocyclic compounds of great biological value.

It has also been reported that the introduction of an alkyl chain into a heterocyclic ring increases its lipophilicity and hence enhances its biological activity. Literature survey has revealed good number of examples where benzotriazole has been N-alkylated using different alkylating agents and the resulting product(s) have found important place in medicinal chemistry [11,12]. Literature also showed that if aliphatic and heterocyclic secondary amines are introduced in a variety of heterocyclic compounds, the resulting compounds have been found to possess enhanced biological activities [13,14]. Thus the aim of the current research was to synthesize *N*-aminoalkylated derivatives of benzo[*d*][1,2,3]triazole possessing alkyl chain, to introduce sufficient lipophilicity, in the molecule so that it may be able to penetrate deep into the membrane along with some polar amino groups at the terminal position of the chain so that compounds may still possess sufficient aqueous solubility to be able to interact with pathogens in aqueous solutions.

2. MATERIALS AND METHODS

2.1 General conditions

1,6-dibromohexane and all heterocyclic secondary amines were purchased from Merck whereas all the aliphatic secondary amines from Aldrich chemicals. All the other used reactants, reagents and solvents were obtained from commercial sources and were of analytical grade. All melting points were determined on an electronic apparatus and are uncorrected. IR spectra were recorded on Shimadzu model IR-435 spectrophotometer using KBr discs for solids and thin films for liquids. ^{1}H NMR and ^{13}C NMR spectra were recorded on Jeol AC (400MHz) and Jeol AC (100 MHz) respectively in $CDCl_3$ using tetramethylsilane (TMS) as an internal standard. TOF ES+ Mass spectra (m/z) were recorded on Micro mass Autospec LCTKC455.

2.2 Synthesis

2.2.1 Synthesis of 1*H*-Benzo[*d*][1,2,3]triazole (2) [15]

To the mixture of 12.0g (11.5mL,0.2mol) of glacial acetic acid and 30mL of water, 10.8 g (0.10mol) of *o*-phenylenediamine (1) was added. The contents were slight warmed and then cooled to 15℃ and stirred it. Then a solution of 7.59g (0.11mol) of sodium nitrite was added to the stirred reaction mixture. The reaction mixture attained the temperature to 85℃ within 2-3 minutes and then slowly begins to cool and changed the color from deep red to pale brown. The stirring was continued till temperature reached down to 35-40℃ and then contents were again stirred in ice-bath for 30 minutes. The pale brown solid that separated out was filtered and washed by ice cold water to give 1*H*- benzo[*d*][1,2,3]triazole. Yield 9.51g (80%);mp99-100℃ [16];R_f=0.51, petroleum ether/ethylacetate (80:20) as a developing solvent; IR(KBr,cm^{-1})ν_{max}:3300,2849,1614,1481,1404,1308,1267,1209,1145,1094,1006,740. ^{1}H NMR(δ,$CDCl_3$,400 MHz): 8.46 (brs,1H,-NH,D_2O exchangeable), 7.92-7.89=(m,2H), 7.41-7.37(m,2H); ^{13}C NMR(δ,$CDCl_3$,100MHz):138.7,126.0,114.8; Mass Spectral data, TOF ES+m/z (%):120(M^++1).

2.2.2 Synthesis of 2-(6-Bromohexyl)-2*H*-benzo[*d*][1,2,3]triazole (3)

1*H*-Benzo[*d*][1,2,3]triazole (2) (5.0g,42.01mmol) was reacted with 1,6-dibromohexane (30.75g,126.05mmol) in the presence of potassium carbonate (17.42g, 126.05mmol) in DMF at 0℃ to room temperature and stirring was continued at room temperature for 12h. Progress of the reaction was monitored on TLC. After the reaction was over, reaction was poured in ice water and then extracted with ethylacetate. The organic layer was dried over anhydrous sodium sulfate and the solvent was evaporated under vacuum. The residue left was purified by column chromatography using silica gel as an adsorbent to obtain 2-(6-bromohexyl)-2*H*-benzo[*d*][1,2,3]triazole (3) as one of the major product. Yield 8.28g (70%); R_f=0.56, petroleum ether/ethylacetate (80:10) as a developing solvent; IR (film,cm^{-1})ν_{max}: 2938, 2859, 1567, 1460, 1438, 1327, 1281, 1129, 979, 850, 748; ^{1}HNMR(δ,$CDCl_3$,400MHz): 7.87-7.84 (m,2H), 7.36-7.34(m,2H), 4.71(t,2H,*J*=7.68Hz,-NCH_2), 3.34(t,2H,*J*=6.6Hz,-CH_2Br), 2.15-2.07(m,2H), 1.84-1.76(m,2H), 1.48-1.32(m,4H); ^{13}CNMR(δ,$CDCl_3$,100MHz): 144.2, 126.2, 117.9, 56.3(-NCH_2), 33.5(-CH_2Br), 32.4, 29.8, 27.5, 25.7; Mass Spectral data, TOF ES+m/z (%): 284(M^++2).

2.2.3 General procedure for the synthesis of title compounds 4a–f

To the mixture of fused K_2CO_3(3.0equiv.) and heterocyclic amines (0.060g, 0.709mmol) in 10mL of dimethylformamide, 2-(6-bromohexyl)-2*H*-benzo[*d*][1,2,3]triazole (3) (0.200g, 0.709mmol) was added slowly `under nitrogen atmosphere. The reaction mixture was heated at 60℃ for 10h. Progress of the reaction was monitored on TLC. After the reaction was over, contents were cooled, quenched with ice water and then extracted with ethylacetate. The organic layer was dried over anhydrous sodium sulfate and the solvent was evaporated under vacuum. The residue left was purified by column chromatography using silica gel as an adsorbent to obtain the desired product 4a-f. Characterization data of 4a-f are given below.

2.2.3.1 2-(6-(Piperidin-1-yl)hexyl)-2H-benzo[d][1,2,3]triazole (4a)

Yield 78%; IR (film,cm^{-1})ν_{max}: 2929, 2855, 2808, 1448, 1327, 1279, 1118, 915, 1070, 864, 748; ^{1}H NMR (δ,$CDCl_3$,400MHz): 7.87-7.85(m,2H), 7.39-7.36(m,2H), 4.73(t,2H,*J*=6.6Hz, -NCH_2), 3.70-3.68(m,4H,2xNCH_2), 2.42-2.38(m,4H), 2.29 (t,2H,*J*=7.32Hz,CH_2-N<), 2.14-2.10(m,2H), 1.49-1.45(m,2H), 1.36-1.25(m,6H); ^{13}C NMR(δ,$CDCl_3$,100MHz): 144.2, 126.1, 117.9, 58.8, 56.4, 53.6, 29.9, 28.4, 26.8, 26.4, 26.2, 24.3; Mass Spectral data, TOF ES+m/z (%): 287(M^++1).

2.2.3.2 2-(6-(Morpholin-4-yl)hexyl)-2H-benzo[d][1,2,3]triazole (4b)

Yield 81%; IR (film,cm^{-1})ν_{max} : 2925, 2853, 2807, 1656, 1448, 1325, 1279, 1117, 1069, 914, 864, 748; ^{1}H NMR (δ, $CDCl_3$,400 MHz): 7.81-7.78 (m,2H), 7.33-7.19 (m,2H), 4.66 (t, 2H,*J*=6.6Hz, -NCH_2), 3.63 (t,4H, -CH_2-O-CH_2), 2.36-2.32 (m,4H, -CH_2-N-CH_2), 2.22 (t,2H *J*=7.32 Hz,CH_2-N<), 2.08-2.04 (m,2H), 1.42-1.37 (m,2H), 1.34-1.14 (m,4H); ^{13}C NMR (δ,$CDCl_3$,100 MHz): 144.2, 126.1, 117.9, 66.9, 58.8, 56.5, 53.7, 29.9, 26.8, 26.4, 26.2; Mass Spectral data, TOF ES+m/z (%): 289 (M^++1).

2.2.3.3 2-(6-(Pyrrolidin-1-yl)hexyl)-2H-benzo[d][1,2,3]triazole (4c)

Yield 77%; IR (film,cm^{-1})ν_{max}: 2928, 2856, 1569, 1459, 1326, 1281, 1145, 980, 851, 747; ^{1}H NMR (δ,$CDCl_3$,400MHz): 7.87-7.85(m,2H), 7.39-7.36(m,2H), 4.72(t,2H,*J*=6.6Hz,-NCH_2), 2.47-2.45(m,4H,-CH_2-N-CH_2), 2.41(t,2H,*J*=7.32Hz,CH_2-N<), 2.14-2.11(m,2H), 1.77-1.75(m, 4H), 1.52-1.49(m,2H), 1.39-1.37(m,4H) ; ^{13}C NMR (δ,$CDCl_3$,100 MHz): 144.1, 126.0, 117.8, 56.4, 54.0, 29.8, 28.4, 26.9, 26.3, 23.2; Mass Spectral data, TOF ES+m/z (%):273 (M^++1).

2.2.3.4 2-(6-(4-Methylpiperazin-1-yl)hexyl-2H-benzo[d][1,2,3]triazole (4d)

Yield 82%; IR (film,cm^{-1})ν_{max}: 2930, 2852, 2795, 1567, 1459, 1326, 1282, 1166, 1014, 747; ^{1}HNMR (δ,$CDCl_3$,400MHz): 7.78-7.75(m,2H), 7.29-7.27(m,2H), 4.63(t,2H,*J*=6.6Hz,-NCH_2), 2.36-2.32(m,4H,-CH_2-N-CH_2), 2.20(t,2H,*J*=7.32Hz,CH_2-N<), 2.17(s,3H), 2.14-2.10(m,4H), 2.04-2.01(m,2H), 1.40-1.38(m,2H), 1.27-1.16(m,4H); ^{13}C NMR (δ,$CDCl_3$,100MHz): 144.2, 126.1, 117.9, 58.4, 56.4, 55.0, 53.1, 45.9, 29.9, 28.3, 26.9, 26.4; Mass Spectral data, TOF ES+m/z (%):302 (M^++1).

2.2.3.5 2-(6-(Isoindolin-2-yl-1,3-dione)hexyl)-2H-benzo[d][1,2,3]triazole (4e)

Yield: 85%; mp 65-67°C; IR (KBr,cm^{-1})ν_{max}: 2925, 2854, 1772, 1710, 1437, 1396, 1328, 1187, 1056, 748, 719; ^{1}HNMR (δ,$CDCl_3$,400MHz): 7.83-7.78 (m,4H), 7.69-7.66(m,2H), 7.36-7.32 (m,2H), 4.69(t,2H,*J*=6.6Hz,-NCH_2), 3.63(t,2H,*J*=7.32Hz, $(CO)_2$N-CH_2), 2.12-2.07(m, 2H), 1.67-1.62(m,2H), 1.39-1.36(m,4H) ; ^{13}C NMR(δ,$CDCl_3$,100 MHz):168.3, 144.1, 133.8, 132.0, 126.1, 123.1, 117.8, 56.3, 37.7, 29.8, 28.3, 26.8, 26.0; Mass Spectral data, TOF ES+ m/z (%):349 (M^++1).

2.2.3.6 2-(6-(1H-Benzo[d]imidazol-1-yl)hexyl)-2H-benzo[d][1,2,3]triazole (4f)

Yield: 83%; IR (film,cm^{-1})ν_{max}: 2920, 2851, 1459, 1300, 1253, 1200, 1005, 949, 867, 742; ^{1}H NMR(δ,$CDCl_3$,400MHz): 7.86-7.81(m,4H), 7.37-7.35(m,3H), 7.27-7.24 (m,2H), 4.68 (t,2H, *J*=6.6Hz,-NCH_2), 4.07 (t,2H,*J*=7.32Hz), 2.11-2.04(m,2H), 1.85-1.78(m,2H), 1.35-1.32(m,

4H); ^{13}C NMR(δ,$CDCl_3$,100MHz): 144.2, 126.2, 122.8, 122.0, 120.3, 117.8, 109.5, 56.2, 44.7, 29.6, 28.4, 26.8, 25.9; Mass Spectral data, TOF ES+m/z (%):320(M^++1).

2.2.4. General procedure for the synthesis of title compounds 4g–j

To the mixture of NaH (0.051g,2.12mmol) and aliphatic secondary amine (0.068g, 0.709mmol) in 10mL of dimethyl formamide, 2-(6-bromohexyl)-2*H*-benzo[*d*][1,2,3]triazole (3) (0.200g,0.709mmol) was added under inert atmosphere and the mixture was heated at 60℃ for 12h. Resulting mixture was poured in ice cold water and extracted with diethylether thrice. Ethereal solutions were combined and dried over anhydrous sodium sulfate. Solvent was removed under vacuum and the resulting residue was purified by column chromatography using silica gel as an adsorbent to yield the desired product 4g-j. Characterization data of 4g-j are given below.

2.2.4.1 2-(N,O-dimethyl-6-aminohexyl)-2H-benzo[d][1,2,3]triazole (4g)

Yield 75%; IR (film,cm^{-1})ν_{max}: 2930, 2951, 2870, 1452, 1344, 1305, 1247, 1149, 1085, 740; ^{1}H NMR(δ,$CDCl_3$,400MHz): 7.87-7.85(m,2H), 7.39-7.37(m,2H), 4.73 (t,2H,*J*=6.6Hz,-NCH_2), 3.48 (s,3H,-OCH_3) 2.54 (s,3H,-NCH_3), 2.13(t,2H,-CH_2-N<), 1.58-1.52(m,2H), 1.44-1.38 (m,2H), 1.29-1.25(m,4H); ^{13}C NMR (δ,$CDCl_3$,100MHz): 144.1, 126.1, 117.8, 62.4, 59.9, 56.4(-NCH_2), 45.1, 29.9, 29.6, 26.7, 26.4; Mass spectral data, TOF ES+*m/z* (%):263(M^++1).

2.2.4.2 2-(N,O-methyl-6-aminohexyl)-2H-benzo[d][1,2,3]triazole (4h)

Yield 79%; IR (film,cm^{-1})ν_{max}: 3401, 3240, 2926, 2855, 1642, 1466, 1421, 1342, 1291, 1241, 1147, 1128, 1084, 1002, 724, 689; ^{1}H NMR (δ, $CDCl_3$, 400 MHz): 7.85-7.83 (m,2H), 7.38-7.36 (m,2H), 4.72 (t,2H,*J*=6.6Hz,-NCH_2), 3.73(s,3H,-OCH_3), 2.40 (t,2H,-CH_2-N<), 2.14-2.16(m,2H), 1.52-1.54(m,2H), 1.43-1.34(m,4H) ; Mass spectral data, TOF ES+*m/z* (%):249 (M^++1).

2.2.4.3 2-(N-hydroxy-N-methyl-6-aminohexyl)-2H-benzo[d][1,2,3]triazole (4i)

Yield 76 %; IR (film,cm^{-1})ν_{max}: 3410, 2926, 2853, 1592, 1444, 1413, 1375, 1251, 1220, 1128, 1044, 772; ^{1}HNMR (δ,$CDCl_3$,400 MHz):7.75-7.73(m,2H), 7.26-7.24(m,2H), 4.61(t,2H,*J*=6.6Hz,-NCH_2), 2.89 (brs,1H,D_2Oexchangeable,-OH), 2.06-2.00(m,5H,CH_2-N-CH_3), 1.44-1.40(m,2H), 1.30-1.24(m,2H), 1.17-1.15(m,4H) ; ^{13}C NMR (δ,$CDCl_3$,100MHz): 144.1, 126.2, 117.8, 56.3(-NCH_2), 65.5, 45.2, 29.6, 27.1, 26.2, 25.9; Mass spectral data, TOF ES+*m/z* (%): 249 (M^++1).

2.2.4.4. 2-(N,N-dimethyl-6-aminohexyl)-2H-benzo[d][1,2,3]triazole (4j)

Yield 75%; IR (film,cm^{-1})ν_{max}: 2926, 2858, 2766, 1660, 1567, 1465, 1367, 1326, 1281, 1189, 980, 850, 748; ^{1}HNMR(δ,$CDCl_3$,400MHz): 7.75-7.73(m,2H), 7.26-7.24(m,2H), 4.63(t,2H,*J*= 6.6Hz,-NCH_2), 2.13 (t,2H,-CH_2-N<), 2.09(brs,6H,2x-NCH_3), 2.04-2.06(m,2H), 1.36-1.31(m,2H), 1.29-1.14(m,4H) ; ^{13}C NMR(δ,$CDCl_3$,100MHz): 144.2, 126.2, 117.6, 56.4(-NCH_2), 62.5, 45.2, 29.4, 27.2, 26.8, 25.8; Mass spectral data, TOF ES+*m/z* (%):247 (M^++1).

3. RESULTS AND DISCUSSION

3.1. Chemistry

We have successfully synthesized ten novel compounds 4a-j in good yields via 2-(6-bromohexyl)-2*H*-benzo[*d*][1,2,3]triazole (3) by employing the reaction sequences shown in various schemes (Scheme 1, 2 and 3).

The reaction of 1*H*-benzo[*d*][1,2,3]triazole (2) with 1,6 dibromohexane in the presence of K_2CO_3/ DMF yielded light yellow colored oil which was characterized as 2-(6-bromohexyl)-2*H*-benzo[*d*][1,2,3]triazole (3) on the basis of its detailed spectral analysis. The main evidence of its formation came from its ^{1}H NMR spectrum that showed two triplets at δ 4.71 and δ 3.34 each integrating for two protons corresponds to N-CH_2 and CH_2Br respectively. Corresponding peaks in the ^{13}C NMR spectrum were observed at δ 56.3 (NCH_2) and δ 33.5 (CH_2Br) respectively. The aromatic protons of benzo[*d*][1,2,3]triazole nucleus were observed at chemical shift values in the downfield region as two multiplets at δ 7.87-7.84 and δ 7.36-7.34, both integrating for two protons. This pattern of aromatic protons showed a total symmetry in the structure and confirmed that alkylation took place at second position of benzo[*d*][1,2,3]triazole. The corresponding aromatic carbons were observed between δ 144.2-117.9 in its ^{13}C NMR spectrum. Its mass spectrum showed (M^++2) at m/z 284 corresponding to its molecular formula $C_{12}H_{16}BrN_3$. Thus on the basis of above spectral analysis, compound 3 was characterized as 2-(6-bromohexyl)-2*H*-benzo[*d*][1,2,3]triazole Scheme 1.

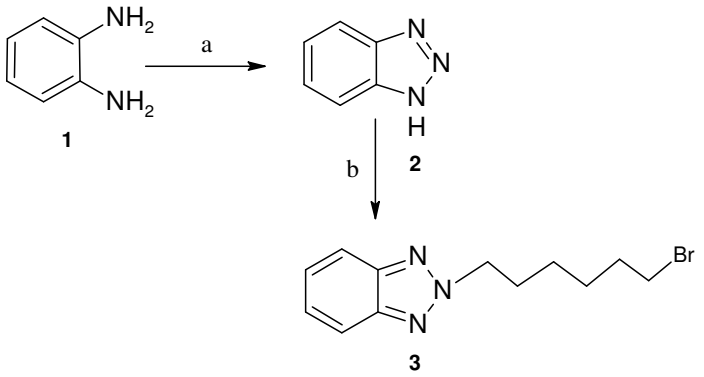
Further, taking the advantage of the presence of the electrophilic center at the end of the chain of the 2-(6-bromohexyl)-2*H*-benzo[*d*][1,2,3]triazole, we coupled it with different aliphatic and heterocyclic secondary amines. The reaction of 2-(6-bromohexyl)-2*H*-benzo[*d*][1,2,3]triazole (3) with piperidine yielded 4a as yellow colored oil. Its mass spectrum showed (M^++1) peak at *m/z* 287, corresponding to the molecular formula $C_{17}H_{26}N_4$, which indicated that piperidine (molecular mass 85) has coupled with 3 (molecular mass 282) with the loss of a HBr molecule. Coupling of the two moieties has been further confirmed by a triplet for two protons at δ 2.29 which was assigned for methylene (CH_2-N<), of the alkyl chain attached to the nitrogen of the piperidine moiety, whereas no peak was observed corresponding to -CH_2Br. Also, its ^{1}H NMR spectrum displayed a multiplet at δ 3.70-3.68 integrating for four protons, assigned to the two methylenes attached to nitrogen of piperidine ring. Corresponding peak in the ^{13}C NMR were observed at δ 53.6 respectively. Characteristic triplet at δ 4.73 for two protons in ^{1}H NMR and a peak at δ 56.4 in ^{13}C NMR was assigned for methlyene attached to benzo[*d*][1,2,3]triazole nucleus through nitrogen atom. Rest of the methylenes protons were observed as multiplets between δ 1.49-1.25, while four aromatic protons were appeared at their expected chemical shift values in the downfield region of the spectrum at δ 7.87-7.36. Thus on the basis of above analysis, compound 4a was characterized as 2-(6-(piperidin-1-yl)hexyl)-2*H*-benzo[*d*][1,2,3]triazole Scheme 2.

Similarly, other nine benzo[*d*][1,2,3]triazole derivatives were prepared by the reaction of 2-(6-bromohexyl)-2*H*-benzo[*d*][1,2,3]triazole with different aliphatic and heterocyclic secondary amines Scheme 2 and 3.

3.2. Antimicrobial Activity

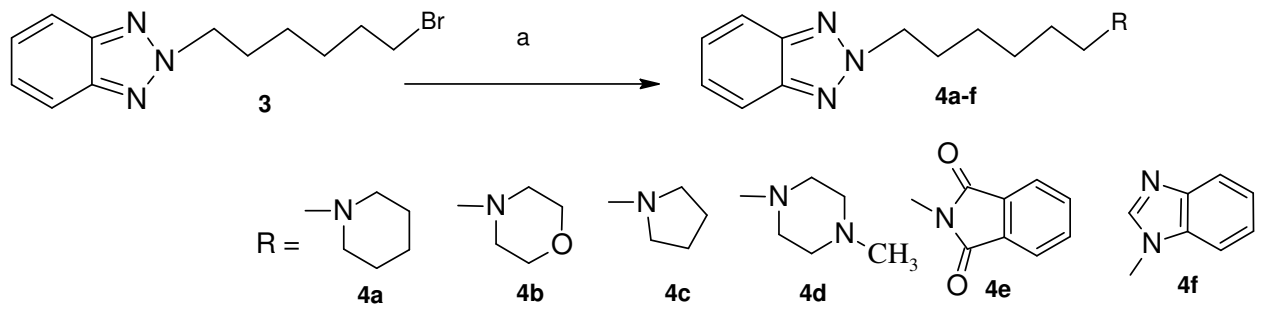
In view of developing new class of antimicrobial agents, synthesized novel compounds were screened for their *In vitro* antimicrobial activities to determine zone of inhibition at 100 µg/mL against three Gram-positive bacteria (*Staphylococcus aureus* (MTCC 096), *Bacillus subtilis* (MTCC 441) and *Staphylococcus epidermis* (MTCC 435)) and four Gram-negative bacteria (*Escherichia coli* (MTCC 443), *Pseudomonas aeruginosa* (MTCC 424), *Salmonella typhi* (MTCC 733) and *Klebsiella pneumoniae* (MTCC 432)) as well as four fungi (*Aspergillus niger* (MTCC 282), *Aspergillus fumigates* (MTCC 343), *Aspergillus flavus* (MTCC 277), and *Candida albicans* (MTCC 227)) strains using Cup plate method [17,18] where inoculated Muller-Hilton agar for bacteria and Sabouraud dextrose agar for fungi was poured onto the sterilized petri dishes (25–30 mL each petri dish). The poured material was allowed to set (30 min.) and thereafter the 'CUPS' (06mm diameter) was made by punching into the agar surface with a sterile cork borer and scooping out the punched part of the agar. Into these cups the test compound solution (0.1mL) was added with the help of a micro pipette. The plates were incubated at 37℃ for 14h for bacteria and 30 h for fungi and the results were noted. The test solution was prepared by DMSO as solvent. Clinically antimicrobial drugs Ciprofloxacin and Miconazole were used as the positive control and DMSO was used for blank.

The obtained results, depicted in Table 1, revealed that all the synthesized compounds, 3 and 4a-j could effectively, to some extent, inhibit the growth of all tested strains *In vitro*. In antibacterial studies, all the compounds tested were found less active towards *Bacillus subtilis, Salmonella typhi*, and *Klebsiella pneumoniae* as compared to other four strains of bacteria. Most of the compounds showed moderate to good activity against *Staphylococcus epidermis, Staphylococcus aureus, Pseudomonas aeruginosa and Salmonella typhi.* Compounds 3, 4h and 4i have shown good antibacterial activity against *Staphylococcus aureus.* 4a and 4b showed good antibacterial activity against *Staphylococcus epidermis.* 4a, 4b and 4i have shown moderate activity against *Escherichia coli.* Out of four strains of fungi, these compounds were found to be less active against *Aspergillus niger* and *Aspergillus flavus* whereas showed moderate to good activity against *Aspergillus fumigatus* and *Candida albicans*. Compounds 3, 4a, 4d, 4e, 4g, 4i and 4j possessed good antifungal activity against *Aspergillus fumigatus* whereas compounds 4d, 4e, 4g and 4j showed moderate activity against *Candida albicans.*



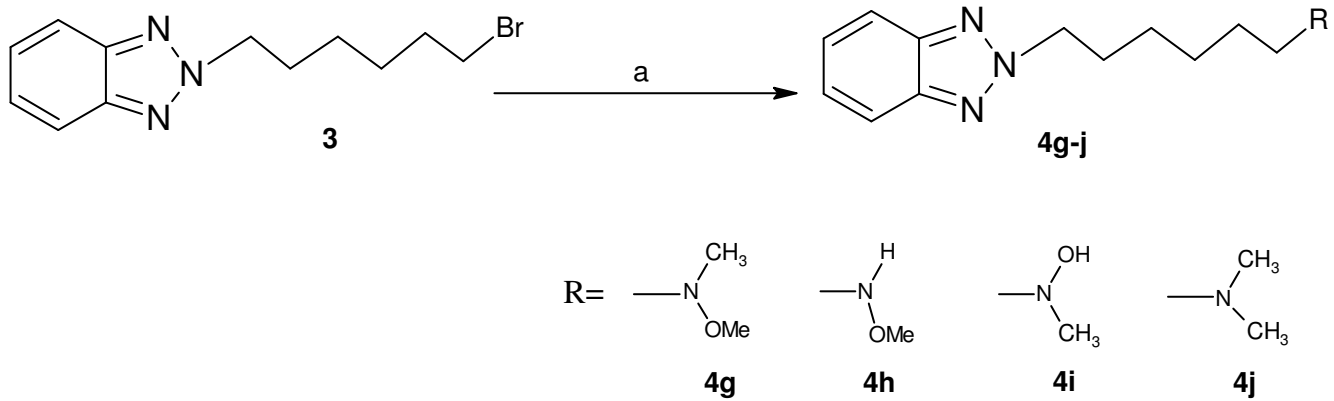
a: $NaNO_2$ / Acetic acid / H_2O; b: 1,6 Dibromohexane, K_2CO_3 / DMF / 0 ^oC -rt

Scheme 1. Synthesis of 2-(6-Bromohexyl)-2*H*-benzo[*d*][1,2,3]triazole



a: Secondary amine / K_2CO_3 / DMF

Scheme 2. Synthesis of title compounds 4a–f



a: Secondary amine / NaH / DMF

Scheme-3. Synthesis of title compounds 4g–j

Table 1. Antimicrobial activity of title compounds 3 and 4a-j

S. No.	Compound	Gram positive bacteria			Gram negative bacteria				Fungi		
		S. aureus	*B. subtilis*	*S. epidermis*	*E. coli*	*P. aeuroginosa*	*S. typhi*	*K. pneumoniae*	*A. niger*	*A. fumigatus*	*A. flavus*	*C. albicans*
1	3	15	12	12	11	13	11	11	11	18	10	16
2	4a	13	12	14	15	12	11	12	10	18	11	14
3	4b	14	10	14	15	12	12	11	11	15	10	18
4	4c	12	10	10	11	11	11	10	12	15	10	14
5	4d	13	11	12	12	11	12	10	12	18	10	18
6	4e	13	10	13	10	11	10	11	11	18	10	18
7	4f	14	11	10	14	13	11	11	13	16	13	14
8	4g	13	10	13	12	12	11	10	13	18	10	18
9	4h	16	10	12	14	14	12	11	10	16	12	16
10	4i	15	13	12	16	13	11	12	14	18	10	16
11	4j	13	11	13	13	13	11	11	13	18	10	18
12	Std[#]	21	20	20	22	20	20	21	29	22	25	30

 # Standard drug for bacteria: Ciprofloxacin; Standard drug for fungi: Miconazole Zone of Inhibition (Internal diameter: 6mm)All the compounds were screened at 100µg/mL concentration.

4. CONCLUSION

We have successfully synthesized ten novel *N*-aminoalkylated derivatives of benzo[*d*][1,2,3]triazole 4a-j containing heterocyclic aliphatic/aromatic amines at the end of the lipophilic chain, in good yields. The structures of all the compounds were confirmed by their spectral data. All the newly synthesized compounds were screened for their MIC and zone of inhibition against seven strains of bacteria and four strains of fungi. Amongst the compounds screened, most of the compounds have shown moderate to good antibacterial and antifungal properties whereas some compounds have shown promising antifungal properties, which were further used to determine MBC and MFC against some selected strains of bacteria and fungi. It is also suggested that *N*-aminoalkylated derivatives of benzo[*d*][1,2,3]triazole are worthy for further investigations as potential antimicrobial agents.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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